Preface

This Committee was created pursuant to SB 322 and section125118.5 of the California Health and Safety Code to provide advice to the Department of Health Services in its development of guidelines for research involving the derivation and use of human embryonic stem cells. In September 2006, SB 1260 became law. It continued the requirement that the Department create such guidelines and added statutory requirements concerning the use of Stem Cell Research Oversight Committees (SCRO Committees) and the process of oocyte donation. The Legislature recognized that the passage of Proposition 71 in November 2004 would lead to the funding of some stem cell research by the California Institute for Regenerative Medicine (CIRM) that was subject to the requirements of that Proposition but not to other California statutes. This Committee is to provide advice on guidelines to govern research not funded by CIRM, but Section 125119(a)(2), as amended by SB 1260 wisely provides that such guidelines should "avoid inconsistencies for stem cell research oversight committees established pursuant to this article with other existing standards for research conducted in California." We have therefore attempted to be consistent whenever possible with the proposed CIRM regulations governing stem cell research.

At this time, in September 2006, CIRM has published for comment proposed regulations. The comment period has closed and CIRM has published for additional comment three sets of revisions to some of those proposed regulations. A copy of what we believe to be the current version of the CIRM regulations, if those revisions are all adopted, is attached.

One inconsistency that we could not reconcile deals with the different scopes of SB 322 and SB 1260, on the one hand, and Proposition 71 and CIRM's regulations, on the other hand. The legislation we deal with requires guidelines covering "the derivation and use of human embryonic stem cells in California." Proposition 71 and CIRM's regulations deal more broadly with any CIRM-funded research dealing with human stem cells, whether or not those are human "embryonic" stem cells. We would note that Section 125300 of the Health and Safety Code, as amended by SB 1260, states that

> "The policy of the State of California shall be that research involving the derivation and use of human embryonic stem cells, human embryonic germ cells, and human adult stem cells, including somatic cell nuclear transplantation, shall be reviewed by a stem cell research oversight committee."

The statutes, however, do not direct the Department to issue guidelines except for human *embryonic* stem cell research and hence our advice is limited to such research. We believe the Department should consider seriously applying these guidelines to some research with human stem cells that are not human embryonic stem cells, particularly human embryonic germ cells or any human stem cells that are pluripotent.

Both SB 1260 and the CIRM regulations require review and approval of the research they cover by SCRO Committees. Federal law, through the so-called

"Common Rule," will also require in most instances that such research, when it is "human subjects research," also be reviewed and approved by Institutional Review Boards (IRBs). In addition, SB 253, passed in 2002 before either SB 322 or SB 1260, created section 125115 of the Health and Safety Code, which provides

> 125115. The policy of the State of California shall be as follows:
>
> (b) That research involving the derivation and use of human embryonic stem cells, human embryonic germ cells, and human adult stem cells, including somatic cell nuclear transplantation, shall be reviewed by an approved institutional review board.

This section does not appear to have been amended or repealed by the subsequent acts, so even human stem cell research that is not "human subjects research" for purposes of federal regulations, be reviewed by an IRB. Therefore, research involving the derivation or use of human embryonic stem cells, with which we deal, will have to be reviewed and approved by both an SCRO Committee and an IRB. We have thus considered the respective strengths of those institutions in recommending the duties of each. The SCRO Committees are likely to have more expertise on stem cell research than the IRBs, which cover a very broad range of research, and so we have assigned issues where such expertise would be particularly useful to the SCRO Committee.

The CIRM regulations, which broadly implement the recommendations of the National Academy of Science's 2005 report, Guidelines for Human Embryonic Stem Cell Research, cover most of the issues relevant to our mission. Neither the CIRM regulations, nor the NAS report, cover in any detail clinical trials using human embryonic stem cells or cells derived from them. The CIRM regulations do briefly discuss SCRO Committee responsibilities when stem cells are to be put inside born alive humans at §100070(f), but they do not focus specifically on clinical trials or their special requirements. It is in this area that our recommendations have concentrated; only technical changes are needed to the CIRM proposed regulations in other areas. We discuss our recommended guidelines for clinical trials first, then discussed other issues.

Guidelines for Clinical Trials Involving Human Embryonic Stem Cells

1. All clinical trials involving the use of human embryonic stem cells or materials derived from human embryonic stem cells, through cell differentiation or otherwise, shall be reviewed and approved by a Stem Cell Research Oversight (SCRO) committee before commencement.

   a. The designated SCRO Committee shall ensure that adequate scientific and ethical review of each protocol has taken place.

   b. The SCRO Committee shall require that investigators

i. Establish that there is sufficient institutional strength in the field to justify conducting such research, particularly with to trials involving the first time particular kinds of cells are being transplanted into humans for particular diseases or in particular organ systems.

ii. Establish that there is sufficient knowledge of the risks and benefits associated with the proposed intervention that it is reasonable to proceed in human populations;

iii. Provide justification that the risks of the trial have been minimized and are reasonable in relation to the anticipated benefits of the trial, including benefits from the generalizable knowledge to be gained.

iv. Address the issue of the diversity of the research subject population, including a justification for why under-represented groups (women, minorities, children) are not included.

c. The SCRO Committee may require, for safety reasons, the testing or screening of donors of the biological materials used in the trial (oocytes, sperm, somatic cells) prior to its commencement.

2. All clinical trials involving the use of human embryonic stem cells or cells differentiated from human embryonic stem cells shall be reviewed and approved by an Institutional Review Board (IRB) before commencement.

a. IRBs shall require that informed consent for any clinical trials involving hESCs and their derivatives include information about where the materials originated from and how they were produced.

b. IRBs shall ensure that the language used in informed consent for early phase clinical trials involved hESCs and their derivatives do not convey an unrealistic impression of the direct benefit of trial participation.

i. The expression “therapeutic cloning” shall not be used to describe any Phase I clinical trials.

c. IRBs shall require that any clinical trials involving hESCs and their derivatives shall have a Data Safety Monitoring Board established to periodically review outcomes and safety of the trial and provide a monitoring plan for the trial.

3. No hESCs shall be placed into human embryos that are going to be used with the intent to create an infant.

Other Guidelines for Research Involving Human Embryonic Stem Cells

The Committee is in general agreement with CIRM's proposed regulations. Where we may differ, the differences seem insufficient to justify having inconsistent regulations. We therefore recommend that the Department adopt the CIRM regulations as guidelines, after adapting them from a funding agency's regulations to these guidelines for all research not funded by CIRM.

The main changes needed are as follows.

Section 100010. Scope of Chapter 2 – Stem Cell Research.

Change the scope from CIRM-funded projects to our statutory language.

Section 100020. Definitions.

Revise definitions as needed. The most important change is in subsection (c), covered stem cell line, which if restricted to our statutory authorization, would only deal with human embryonic stem cells.

Section 100030. Activities Not Eligible for CIRM Funding.

This section should be revised to state the subsections as banned activities, not merely as things that will not be funded.

Section 100040. Institutional Assurance of Compliance.

Unchanged

Section 100050. Compliance.

This should be replaced by a discussion of whatever enforcement methods the Department chooses to use to enforce these guidelines.

Section 100060. SCRO Committee Membership and Function.

Unchanged.

Section 100070. SCRO Committee Review and Notification.

Unchanged except for deleting references to "CIRM-funded research".

Section 100080. Acceptable Research Materials.

Unchanged except for deleting references to "CIRM-funded research".

Section 100090. Additional Requirements for CIRM-Funded Derivation.

Unchanged except for deleting references to CIRM funding.

Section 100095. Additional Requirements for CIRM-Funded Research Involving Oocytes.

Unchanged except for deleting references to "CIRM-funded research".

Section 100100. Informed Consent Requirements.

Unchanged except for deleting references to "CIRM-funded research".

Section 100110. Fairness and Diversity in Research.

Unchanged except for deleting references to "CIRM funded".

Section 100120 - Record Keeping.

Unchanged except for deleting references to "CIRM-funded research".